Data Sheet (Cat.No.T4689)

TargetMol

Palosuran hydrochloride 540769-28-6(free base)

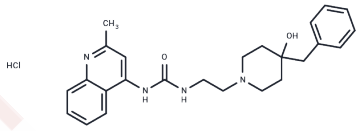
Chemical Properties

CAS No. :

Formula: C25H31ClN4O2

Molecular Weight: 454.99

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.



Biological Description

Description	Palosuran hydrochloride 540769-28-6(free base)(ACT-058362 hydrochloride) is a new potent and specific antagonist of the human UT receptor with an IC50 of 3.6±0.2 nM.
Targets(IC50)	GPCR
In vitro	Palosuran inhibited 125I-U-II binding to human UT receptors in membrane preparations from CHO cells carrying the human UT receptors almost as potently as cold U-II, with an IC50 of 3.6 ± 0.2 nM. On cells, the inhibitory binding potency of palosuran against human UT receptor was lower than on membranes (IC50 = 46.2 ± 13 nM on TE 671 cells and 86 ± 30 nM on recombinant CHO cells). Compared with the human UT receptor, the binding inhibitory potency of palosuran against the rat UT receptor was lower in membrane preparation (400-fold), as well as in cells (>120-fold) [1].
In vivo	Long-term treatment of streptozotocin-induced diabetic rats with palosuran improved survival, increased insulin, and slowed the increase in glycemia, glycosylated hemoglobin, and serum lipids. Furthermore, palosuran increased renal blood flow and delayed the development of proteinuria and renal damage [2]. Palosuran was rapidly absorbed with maximum plasma concentrations at 1 hour after drug administration. The accumulation factor was 1.7 (geometric mean) (95% confidence interval, 1.3 to 2.1). Palosuran was well tolerated [3]. In mesenteric vessels, palosuran treatment up-regulated expression of RhoA and Rho-kinase, increased Rho-kinase-activity, and diminished nitric oxide (NO)/cyclic guanosine 3',5'-monophosphate (cGMP) signaling. Moreover, palosuran increased renal blood flow, sodium, and water excretion in BDL rats [4].

Solubility Information

Solubility	DMSO: >30 mg/mL,Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1979 mL	10.9893 mL	21.9785 mL
5 mM	0.4396 mL	2.1979 mL	4.3957 mL
10 mM	0.2198 mL	1.0989 mL	2.1979 mL
50 mM	0.044 mL	0.2198 mL	0.4396 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Clozel M, et al. Pharmacology of the urotensin-II receptor antagonist palosuran (ACT-058362; 1-[2-(4-benzyl-4-hydroxy-piperidin-1-yl)-ethyl]-3-(2-methyl-quinolin-4-yl)-urea sulfate salt): first demonstration of a pathophysiological role of the urotensin System.[J]. J Pharmacol Exp Ther, 2004, 311(1):204-212.
Clozel M, et al. The urotensin-II receptor antagonist palosuran improves pancreatic and renal function in diabetic rats. J Pharmacol Exp Ther. 2006 Mar;316(3):1115-21.
Sidharta PN, et al. Pharmacodynamics and pharmacokinetics of the urotensin II receptor antagonist palosuran in macroalbuminuric, diabetic patients. Clin Pharmacol Ther. 2006 Sep;80(3):246-56.
Trebicka J, et al. Hemodynamic effects of urotensin II and its specific receptor antagonist palosuran in cirrhotic rats. Hepatology. 2008 Apr;47(4):1264-76.